REMARKS

Claims 1-3 are pending in the instant application. Claim 1-3 have been rejected. Claim 1 has been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. §103

The Examiner has maintained the rejection of claims 1-3 under 35 U.S.C. §103(a) as being unpatentable over Coligan et al. (Current Protocols in Immunology, Green Publishing Associates and Wiley-Interscience, New York, 1991; pages 2.1.1-2.1.3, 2.1.9-2.1.11, and 2.1.17-2.1.22) in view of U.S. Patent 5,077,216, Zwaldo et al. (1987) (IDS Reference BA), and Zwaldo et al. (1992) (IDS Reference AX) for the reasons set forth in the Office Action mailed 10/5/04.

The Examiner suggests that Applicants arguments to this rejection are not persuasive because Zwaldo et al. (IDS Reference BA) teach that the RM3/1 antigen (*i.e.*, CD163 antigen) is useful for monitoring an early signaling event in an inflammatory response in a patient. The Examiner suggests that Zwaldo et al. do not teach away from the instant invention as Zwaldo et al. teach that levels of RM3/1 antigen reach maximum levels late in the inflammatory response and that, depending on the state of inflammation (pages 299, 301, and 303), RM3/1 antigen is expressed at different levels. It is suggested that Zwaldo et al. explicitly teach that in acute inflammation, *i.e.*, early in an inflammatory response, RM3/1 antigen is expressed to varying degree, depending on the stage of inflammation. In addition, the Examiner suggests that Zwaldo et al. (IDS Reference AX) teach

monitoring the appearance of RM3/1 positive macrophages in blood between 24 and 72 hours post-inflammatory response. Further, it is suggested that it would have been obvious to use the MAC2-158 and MAC2-48 antibodies as capture antibodies taught in the '216 patent and the antibodies taught by Zwaldo et al. as the detection antibody in the ELISA taught by Coligan et al. to have a method for monitoring the course of an inflammatory condition or inflammatory response in a patient by detecting the levels of CD163 in a biological sample as taught by Zwaldo et al. Moreover, the Examiner suggests that the teachings of Arondel et al. are irrelevant for the instant application, since the instant claims do not recite measuring the ratio between inductive and inhibitory signals. Applicants respectfully disagree with this rejection.

Applicants respectfully disagree with the Examiner's interpretation of the teachings of Zwaldo et al. (IDS Reference BA). Regarding the specific teachings of Zwaldo et al. cited by the Examiner, the paragraph bridging pages 299 and 301 states "[i]n acute inflammatory tissue, e.g. erythroderma and gingivitis (fig. 2e), RM3/1 antigen was found to be expressed to varying degrees, depending on the stage of inflammation. This was most evident in experimental gingivitis, which was induced in volunteers by omitting dental hygiene, or was reduced by tooth cleansing. The stage of inflammation was measurable by clinical indices (e.g. gingival index) [Topoll et al., 1987]. In biopsies at different inflammatory states of gingivitis, high numbers of RM3/1-positive macrophages were correlated with low gingival index, while low numbers of RM3/1-positive macrophages were associated with a high index or stage of inflammation,

respectively (fig. 3)." In this regard, Figure 2e shows the distribution of RM3/1-positive cells in gingivitis with no indication as to when the sample was isolated and Figure 3 shows varying degrees of RM3/1 expression at day -14, day 0, day 2, day 4, day 7, day 11 and day 19 in human experimental gingivitis, wherein RM3/1 expression from day 0 to day 2 decreases from 100 positive cells to 70 positive cells. As such, there is simply no teaching or suggestion of measuring a detectable elevation in the level of CD163 within 1 to 12 hours of exposure to the inflammatory stimulus found at pages 299 and 301 nor in Figures 2e and 3 of Zwaldo et al. Moreover, page 303 of Zwaldo et al. states "[i]n acute inflammatory sites, RM3/1-positive cells are found to varying amounts depending on the state of inflammation. Kinetic studies of gingivitis (fig. 3) indicate that RM3/1 macrophages increase during the healing phase and decrease during onset of inflammation." Thus, based upon these teachings, Applicants find no reasonable basis for the Examiner to conclude that Zwaldo et al. make the instant invention obvious as a whole, because Zwaldo et al. teach that RM3/1 macrophages decrease during onset of acute inflammation, whereas the instant specification teaches that an increase in the level of CD163 is one of the earliest changes induced by an acute inflammatory response that can be detected (see page 11, lines 12-16). Because the insight provided in the instant specification is contrary to the understandings and expectations of the art (MPEP 2141.02), it would not have been obvious to those skilled in the art that elevated levels of CD163 within 1 to 12 hours of exposure to the inflammatory stimulus are indicative of an early signaling event in an inflammatory response cascade in patient. In an earnest

effort to clarify the teachings of the instant application, Applicants have amended claim 1 to indicate that elevated levels of CD163 within 1 to 12 hours of exposure to the inflammatory stimulus are indicative of an early signaling event in an inflammatory response cascade in the patient.

While Arondel et al. ((1999) *Infect. Immun.* 67:6056-6066), is silent to the levels of CD163 in early signaling events, Applicants have provided Arondel et al. as evidence of the general knowledge in the art concerning how rapidly protein expression levels can increase and decrease in an inflammatory response such that measurements taken at 24+ hours after exposure to an inflammatory stimulus (*e.g.*, as taught in Zwaldo et al., IDS References BA and AX) are not indicative of signaling events that occur within 1 to 12 hours of exposure to the inflammatory stimulus. In view of the teachings of Arondel et al., one of skill in the art could not reasonably extrapolate the levels of CD163 at 1 to 12 hours after exposure to an inflammatory stimulus based upon the teachings of Zwaldo et al. (IDS references AB and AX). Therefore, it would not have been obvious to one of skill in the art at the time of filing of the instant application that an elevation in the level of CD163 within 1 to 12 hours of exposure to the inflammatory stimulus is indicative of an early signaling event in the inflammatory response cascade in the patient

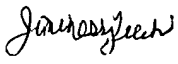
Because Coligan et al. and U.S. Patent 5,077,216 are silent to CD163 expression levels in an inflammatory response and Zwaldo et al. (IDS References AB and AX) fail to provide any teaching, suggestion, or motivation to modify the teachings therein to measure the levels of CD163 within 1 to 12 hours of exposure to an inflammatory stimulus for detecting an early signaling event

in an inflammatory response cascade in a patient, these references fail to establish a *prima facie* case of obviousness as required by MPEP 2143. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

II. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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